28585

Biotech/ChemLib

From: Chan, Christina
Sent: Wednesday, May 10, 2000 8:42 AM
To: STIC-Biotech/ChemLib
Cc: Ungar, Susan
Subject: FW: Rush search for 09/218,481

Importance: High

Please rush. Thanks Chris

-----Original Message-----
From: Ungar, Susan
Sent: Wednesday, May 10, 2000 8:18 AM
To: Chan, Christina
Subject: Rush search for 09/218,481

Hi

I need a rush search for 09/218,481. I would appreciate having this search back by Tuesday, May 16 if at all possible

Please search the following:

A method of treating a mammal having edema comprising administering an anti-VEGF antibody

A method of treating a mammal having cerebral edema comprising administering an anti-VEGF antibody

Please search this with and without the inventors

Nicholas Van Bruggen
Napoleone Ferrara

Please approve this search and forward it on to STIC

Thanks
Susan Ungar
1642
305-2181
CM1-8B05

Point of Contact:
Mary Hale
Technical Info. Specialist
CM1 12D16 Tel: 308-4258

2847

Ungar
218481

```
=> fil reg

COST IN U.S. DOLLARS                                  SINCE FILE      TOTAL
                                                         ENTRY    SESSION
FULL ESTIMATED COST                                       0.15       0.15

FILE 'REGISTRY' ENTERED AT 10:51:34 ON 17 MAY 2000
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
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STRUCTURE FILE UPDATES:   16 MAY 2000  HIGHEST RN 264927-87-9
DICTIONARY FILE UPDATES:  16 MAY 2000  HIGHEST RN 264927-87-9

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 11, 2000

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

Structure search limits have been increased.  See HELP SLIMIT
for details.

=> e edema/cn 5

E1            1     EDELEX 45/CN
E2            1     EDELFOSINE/CN
E3            0 --> EDEMA/CN
E4            1     EDEMATRIN/CN
E5            1     EDEMEX/CN

=> e "anti vegf"/cn 5

E1            1     ANTI SIGMA FACTOR FLGM (AQUIFEX AEOLICUS GENE FLGM)/CN
E2            1     ANTI UV-K/CN
E3            0 --> ANTI VEGF/CN
E4            1     ANTI(2.2)(2,7)FLUORENOPHANE/CN
E5            1     ANTI,ANTI-TRISHOMOCYCLOHEPTATRIENE/CN

=> e vegf/cn 5

E1            1     VEGETATIVE MYCELIUM HYDROPHOBIN 3 (PLEUROTUS OSTREATUS
STRAI
                    N N001 GENE VMH3 PRECURSOR)/CN
E2            1     VEGETOX/CN
E3            0 --> VEGF/CN
E4            1     VEGF (HUMAN 148-AMINO ACID ISOFORM)/CN
E5            1     VEGF (HUMAN 183-AMINO ACID ISOFORM PRECURSOR)/CN

=> fil medl,caplus,biosis,embase,wpids

COST IN U.S. DOLLARS                                  SINCE FILE      TOTAL
                                                         ENTRY    SESSION
FULL ESTIMATED COST                                       0.30       0.45

FILE 'MEDLINE' ENTERED AT 10:52:24 ON 17 MAY 2000

FILE 'CAPLUS' ENTERED AT 10:52:24 ON 17 MAY 2000
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FILE 'BIOSIS' ENTERED AT 10:52:24 ON 17 MAY 2000
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FILE 'EMBASE' ENTERED AT 10:52:24 ON 17 MAY 2000
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FILE 'WPIDS' ENTERED AT 10:52:24 ON 17 MAY 2000
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=> s (?edema? or (brain or cerebral)(w)edema or c23.888.277/ct) and (anti vegf)

L1 2 FILE MEDLINE
L2 2 FILE CAPLUS
L3 1 FILE BIOSIS
L4 2 FILE EMBASE
L5 1 FILE WPIDS

TOTAL FOR ALL FILES
L6 8 (?EDEMA? OR (BRAIN OR CEREBRAL)(W) EDEMA OR C23.888.277/CT) AND
(ANTI VEGF)

=> dup rem l6

PROCESSING COMPLETED FOR L6
L7 3 DUP REM L6 (5 DUPLICATES REMOVED)

=> d cbib abs 1-3 hit

L7 ANSWER 1 OF 3 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD
AN 1999-229406 [19] WPIDS
AB WO 9913909 A UPAB: 19990518
NOVELTY - Corneal neovascularization inhibitors comprise a vascular endothelial growth factor/vascular permeability factor (VEGF/VPF) antagonist.
ACTIVITY - Ophthalmological.
Lewis rats had corneal grafts implanted from Fischer rats. On a scale of 0 (no blood vessel growth) to 3 (blood vessel growth seen without using a microscope) **anti-VEGF**/VPF antibody administered as eyedrops containing 20 mg/ml at 10 mu l/dose 5 times a day for 10 days scored about 1.5, compared to 2.5 for a control and just under 2.5 for IgG given at 14 mg/ml as eyedrops at 10 mu l/dose 5 times a day for 10 days.
MECHANISM OF ACTION - VEGF-Antagonist
USE - As inhibitors of neovascularization in corneitis or corneal grafting useful for preventing corneal clouding or **edematization** and for promoting the take of grafts.
Dwg.0/7
AB WO 9913909 A UPAB: 19990518
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ACTIVITY - Ophthalmological.
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MECHANISM OF ACTION - VEGF-Antagonist

USE - As inhibitors of neovascularization in corneitis or corneal grafting useful for preventing corneal clouding or **edematization** and for promoting the take of grafts.

Dwg.0/7

L7 ANSWER 2 OF 3 MEDLINE DUPLICATE 1

97197752 Document Number: 97197752. Upregulation of vascular endothelial growth factor in ischemic and non-ischemic human and experimental retinal disease. Vinores S A; Youssri A I; Luna J D; Chen Y S; Bhargave S; Vinores M A; Schoenfeld C L; Peng B; Chan C C; LaRochelle W; Green W R; Campochiaro P A. (The Wilmer Opthalmologic Institute, Johns Hopkins University School of Medicine, Baltimore, MD 21287-9289, USA.) HISTOLOGY AND HISTOPATHOLOGY, (1997 Jan) 12 (1) 99-109. Journal code: BEM. ISSN: 0213-3911. Pub. country: Spain. Language: English.

AB Vascular endothelial growth factor (VEGF) is induced by hypoxia and it has been implicated in the development of iris and retinal neovascularization (NV) in ischemic retinopathies in which it has been suggested that Muller cells are responsible for increased VEGF production. VEGF, however, is also known to be a potent mediator of vascular permeability in other tissues and may perform this function in retina. Immunohistochemical staining for VEGF was performed on a variety of human and experimental ischemic and non-ischemic ocular disorders in which blood retinal barrier (BRB) breakdown is known to occur to determine if there is an upregulation of VEGF in these conditions. We found increased VEGF immunoreactivity in ganglion cells of rats with oxygen-induced ischemic retinopathy and in ganglion cells, the inner plexiform layer, and some cells in the inner nuclear layer of rats with experimental autoimmune uveoretinitis (EAU), in which there was no identifiable ischemia or NV. In rats with EAU, VEGF staining intensity increased from 8 to 11 days after immunization, coincident with BRB failure. These results were confirmed using two distinct **anti-VEGF** antibodies and by immunoblot and the immunohistochemical staining was eliminated by pre-incubating the antibodies with VEGF peptide. VEGF staining was also increased in the retina and iris of patients with ischemic retinopathies, such as diabetic retinopathy and retinal vascular occlusive disease, and in patients with disorders in which retinal ischemia does not play a major role, such as aphakic/ pseudophakic cystoid macular **edema**, retinoblastoma, ocular inflammatory disease or infection, and choroidal melanoma. VEGF was primarily localized within retinal neurons and retinal pigmented epithelial cells in these cases. In addition or in association with its role of inducing NV, VEGF may contribute to BRB breakdown in a variety of ocular disorders and blockage of VEGF signaling may help to reduce some types of macular **edema**.

AB Vascular endothelial growth factor (VEGF) is induced by hypoxia and it has been implicated in the development of iris and retinal neovascularization (NV) in ischemic retinopathies in which it has been suggested that Muller cells are responsible for increased VEGF production. VEGF, however, is also known to be a potent mediator of vascular permeability in other tissues and may perform this function in retina. Immunohistochemical

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L7 ANSWER 3 OF 3 MEDLINE DUPLICATE 2

97197647 Document Number: 97197647. Involvement of vascular endothelial growth factor in Kaposi's sarcoma associated with acquired immunodeficiency syndrome. Sakurada S; Kato T; Mashiba K; Mori S; Okamoto T. (Department of Molecular Genetics, Nagoya City University Medical School, Mizuho-ku.) JAPANESE JOURNAL OF CANCER RESEARCH, (1996 Nov) 87 (11) 1143-52. Journal code: HBA. ISSN: 0910-5050. Pub. country: Japan. Language: English.

AB To examine the role of vascular endothelial growth factor (VEGF) in the development of **edema** associated with Kaposi's sarcoma (KS) in acquired immunodeficiency syndrome (AIDS), we exploited animal model systems to detect the activity that induces vascular hyper-permeability (VHP) using cultured AIDS-KS spindle cells. Cultured AIDS-KS spindle cells and conditioned medium (AIDS-KS-CM) that had been semi-purified through a heparin affinity column were tested for the ability to induce VHP in animals. The AIDS-KS spindle cells and AIDS-KS-CM induced VHP that was histamine-independent. The VHP-inducing activity was detected in the 0.5 M NaCl fraction from the heparin affinity column and was blocked by **anti-VEGF** neutralizing antibody. In addition, the production of VEGF was demonstrated in fresh AIDS-KS tissue as well as in cultured AIDS-KS cells, while control cells were negative for VEGF production. From these observations, we concluded that AIDS-KS cells produce a factor(s) that promotes VHP, and this factor could be VEGF.

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histamine-independent. The VHP-inducing activity was detected in the 0.5
M
NaCl fraction from the heparin affinity column and was blocked by
anti-VEGF neutralizing antibody. In addition, the
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cultured AIDS-KS cells, while control cells were negative for VEGF
production. From these observations, we concluded that AIDS-KS cells
produce a factor(s) that promotes VHP, and this factor could be VEGF.
CT Check Tags: Animal; Female; Human; Male; Support, Non-U.S. Gov't
*Acquired Immunodeficiency Syndrome: CO, complications
Acquired Immunodeficiency Syndrome: PP, physiopathology
Capillary Permeability
Cells, Cultured
Chromatography, Affinity
Culture Media
Cytokines: PH, physiology
Disease Models, Animal
Edema: ET, etiology
Edema: PP, physiopathology
*Endothelial Growth Factors: PH, physiology
Guinea Pigs
Heparin
*Lymphokines: PH, physiology
Mice
Mice, Inbred BALB C
Mice, Nude
Middle Age
Rabbits
*Sarcoma, Kaposi: BS, blood supply
*Sarcoma, Kaposi: CI, chemically induced
Sarcoma, Kaposi: VI, virology

=> s van bruggen n?/au,in;s ferrara n?/au,in

'IN' IS NOT A VALID FIELD CODE
L8 31 FILE MEDLINE
L9 10 FILE CAPLUS
L10 41 FILE BIOSIS
'IN' IS NOT A VALID FIELD CODE
L11 30 FILE EMBASE
L12 0 FILE WPIDS

TOTAL FOR ALL FILES
L13 112 VAN BRUGGEN N?/AU,IN

'IN' IS NOT A VALID FIELD CODE
L14 203 FILE MEDLINE
L15 177 FILE CAPLUS
L16 260 FILE BIOSIS
'IN' IS NOT A VALID FIELD CODE
L17 205 FILE EMBASE
L18 16 FILE WPIDS

TOTAL FOR ALL FILES
L19 861 FERRARA N?/AU,IN

=> s l13 and l19

L20 2 FILE MEDLINE

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L21           2 FILE CAPLUS
L22           1 FILE BIOSIS
L23           2 FILE EMBASE
L24           0 FILE WPIDS

TOTAL FOR ALL FILES
L25           7 L13 AND L19

=> s l25 not l6

L26           2 FILE MEDLINE
L27           2 FILE CAPLUS
L28           1 FILE BIOSIS
L29           2 FILE EMBASE
L30           0 FILE WPIDS

TOTAL FOR ALL FILES
L31           7 L25 NOT L6

=> dup rem l31

PROCESSING COMPLETED FOR L31
L32           2 DUP REM L31 (5 DUPLICATES REMOVED)

=> d cbib abs 1-2


L32  ANSWER 1 OF 2  MEDLINE                                  DUPLICATE 1
2000056162  Document Number: 20056162.  VEGF antagonism reduces edema
     formation and tissue damage after ischemia/reperfusion injury in the
mouse
     brain. van Bruggen N; Thibodeaux H; Palmer J T; Lee W P; Fu L;
     Cairns B; Tumas D; Gerlai R; Williams S P; van Lookeren Campagne M;
     Ferrara N. (Department of Neuroscience, Genentech Inc., South San
     Francisco, California 94080, USA.. vanbruggen.nick@gene.com) . JOURNAL OF
     CLINICAL INVESTIGATION, (1999 Dec) 104 (11) 1613-20.  Journal code: HS7.
     ISSN: 0021-9738. Pub. country: United States. Language: English.
AB   VEGF is mitogenic, angiogenic, and a potent mediator of vascular
     permeability. VEGF causes extravasation of plasma protein in skin
     bioassays and increases hydraulic conductivity in isolated perfused
     microvessels. Reduced tissue oxygen tension triggers VEGF expression, and
     increased protein and mRNA levels for VEGF and its receptors (Flt-1,
     Flk-1/KDR) occur in the ischemic rat brain. Brain edema, provoked in part
     by enhanced cerebrovascular permeability, is a major complication in
     central nervous system pathologies, including head trauma and stroke. The
     role of VEGF in this pathology has remained elusive because of the lack
of
     a suitable experimental antagonist. We used a novel fusion protein,
     mFlt(1-3)-IgG, which sequesters murine VEGF, to treat mice exposed to
     transient cortical ischemia followed by reperfusion. Using
high-resolution
     magnetic resonance imaging, we found a significant reduction in volume of
     the edematous tissue 1 day after onset of ischemia in mice that received
     mFlt(1-3)-IgG. 8-12 weeks after treatment, measurements of the resultant
     infarct size revealed a significant sparing of cortical tissue. Regional
     cerebral blood flow was unaffected by the administration of
mFlt(1-3)-IgG.
     These results demonstrate that antagonism of VEGF reduces
     ischemia/reperfusion-related brain edema and injury, implicating VEGF in
     the pathogenesis of stroke and related disorders.
```

L32 ANSWER 2 OF 2 MEDLINE DUPLICATE 2

1998250918 Document Number: 98250918. Magnetic resonance imaging detects suppression of tumor vascular permeability after administration of antibody to vascular endothelial growth factor. Pham C D; Roberts T P; **van Bruggen N**; Melnyk O; Mann J; **Ferrara N**; Cohen R L; Brasch R C. (Department of Radiology, University of California, San Francisco, USA.) CANCER INVESTIGATION, (1998) 16 (4) 225-30. Journal code: CAI. ISSN: 0735-7907. Pub. country: United States. Language: English.

AB Macromolecular contrast medium-enhanced magnetic resonance imaging (MRI) and tumor-volume measurements were applied to monitor the effects of anti-vascular endothelial growth factor (anti-VEGF) antibody on microvascular characteristics and tumor growth of MDA-MB-435 human breast cancer cells implanted in nude rats. Administration of anti-VEGF antibody (three 1 mg doses at 3-day intervals) induced significant reductions in tumor growth rates ($p < 0.05$) and in MRI-assayed microvascular permeabilities ($p < 0.05$). Results of the study were consistent with previous observations that new microvessels formed in response to angiogenesis are hyperpermeable, and with the hypothesis that hyperpermeability is a mechanistic element in angiogenesis. Variations in tumor-vessel hyperpermeability can be measured by contrast-enhanced MRI, which may prove useful for assessing antiangiogenesis therapy.

=> s (l13 or l19)

L33 232 FILE MEDLINE
L34 185 FILE CAPLUS
L35 300 FILE BIOSIS
L36 233 FILE EMBASE
L37 16 FILE WPIDS

TOTAL FOR ALL FILES
L38 966 (L13 OR L19)

=> s (?edema? or (brain or cerebral)(w)edema or c23.888.277/ct) and l38

L39 11 FILE MEDLINE
L40 3 FILE CAPLUS
L41 10 FILE BIOSIS
L42 11 FILE EMBASE
L43 2 FILE WPIDS

TOTAL FOR ALL FILES
L44 37 (?EDEMA? OR (BRAIN OR CEREBRAL)(W) EDEMA OR C23.888.277/CT) AND L38

=> dis his

(FILE 'HOME' ENTERED AT 10:51:22 ON 17 MAY 2000)

FILE 'REGISTRY' ENTERED AT 10:51:34 ON 17 MAY 2000
E EDEMA/CN 5
E "ANTI VEGF"/CN 5
E VEGF/CN 5

FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, WPIDS' ENTERED AT 10:52:24 ON 17 MAY 2000
L1 2 FILE MEDLINE

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L2             2 FILE CAPLUS
L3             1 FILE BIOSIS
L4             2 FILE EMBASE
L5             1 FILE WPIDS
     TOTAL FOR ALL FILES
L6             8 S (?EDEMA? OR (BRAIN OR CEREBRAL)(W)EDEMA OR C23.888.277/CT)
AN
L7             3 DUP REM L6 (5 DUPLICATES REMOVED)
L8            31 FILE MEDLINE
L9            10 FILE CAPLUS
L10           41 FILE BIOSIS
L11           30 FILE EMBASE
L12            0 FILE WPIDS
     TOTAL FOR ALL FILES
L13          112 S VAN BRUGGEN N?/AU,IN
L14          203 FILE MEDLINE
L15          177 FILE CAPLUS
L16          260 FILE BIOSIS
L17          205 FILE EMBASE
L18           16 FILE WPIDS
     TOTAL FOR ALL FILES
L19          861 S FERRARA N?/AU,IN
L20            2 FILE MEDLINE
L21            2 FILE CAPLUS
L22            1 FILE BIOSIS
L23            2 FILE EMBASE
L24            0 FILE WPIDS
     TOTAL FOR ALL FILES
L25            7 S L13 AND L19
L26            2 FILE MEDLINE
L27            2 FILE CAPLUS
L28            1 FILE BIOSIS
L29            2 FILE EMBASE
L30            0 FILE WPIDS
     TOTAL FOR ALL FILES
L31            7 S L25 NOT L6
L32            2 DUP REM L31 (5 DUPLICATES REMOVED)
L33          232 FILE MEDLINE
L34          185 FILE CAPLUS
L35          300 FILE BIOSIS
L36          233 FILE EMBASE
L37           16 FILE WPIDS
     TOTAL FOR ALL FILES
L38          966 S (L13 OR L19)
L39           11 FILE MEDLINE
L40            3 FILE CAPLUS
L41           10 FILE BIOSIS
L42           11 FILE EMBASE
L43            2 FILE WPIDS
     TOTAL FOR ALL FILES
L44           37 S (?EDEMA? OR (BRAIN OR CEREBRAL)(W)EDEMA OR C23.888.277/CT)
AN

=> s l44 not (l6 or l25)

L45           10 FILE MEDLINE
L46            2 FILE CAPLUS
L47           10 FILE BIOSIS
L48           10 FILE EMBASE
L49            2 FILE WPIDS
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TOTAL FOR ALL FILES
L50 34 L44 NOT (L6 OR L25)

=> dup rem l50

PROCESSING COMPLETED FOR L50
L51 16 DUP REM L50 (18 DUPLICATES REMOVED)

=> d cbib abs 1-16

L51 ANSWER 1 OF 16 MEDLINE DUPLICATE 1
2000006327 Document Number: 20006327. Evidence for a protective role of metallothionein-1 in focal cerebral ischemia. van Lookeren Campagne M; Thibodeaux H; **van Bruggen N**; Cairns B; Gerlai R; Palmer J T; Williams S P; Lowe D G. (Department of Cardiovascular Research, Genentech Inc., 1 DNA Way, South San Francisco, CA 94080, USA.. menno@gene.com) . PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (1999 Oct 26) 96 (22) 12870-5. Journal code: PV3. ISSN: 0027-8424. Pub. country: United States. Language: English.
AB Metallothioneins (MTs) are a family of metal binding proteins that have been proposed to participate in a cellular defense against zinc toxicity and free radicals. In the present study, we investigated whether increased expression of MT in MT-1 isoform-overexpressing transgenic mice (MT-TG) affords protection against mild focal cerebral ischemia and reperfusion. Transient focal ischemia was induced in control (wild type) and MT-TG mice by occluding the right middle cerebral artery for 45 min. Upon reperfusion, **cerebral edema** slowly developed and peaked at 24 hr as shown by T2-weighted MRI. The volume of affected tissue was on the average 42% smaller in MT-TG mice compared with control mice at 6, 9, 24, and 72 hr and 14 days postreperfusion ($P < 0.01$). In addition, functional studies showed that 3 weeks after reperfusion MT-TG mice showed a significantly better motor performance compared with control mice ($P = 0.011$). Although cortical baseline levels of MT-1 mRNA were similar in control and MT-TG mice, there was an increase in MT-1 mRNA levels in the ischemic cortex of MT-TG mice to 7.5 times baseline levels compared with an increase to 2.3 times baseline levels in control mice 24 hr after reperfusion. In addition, MT-TG mice showed an increased MT immunoreactivity in astrocytes, vascular endothelial cells, and neurons 24 hr after reperfusion whereas in control mice MT immunoreactivity was restricted mainly to astrocytes and decreased in the infarcted tissue. These results provide evidence that increased expression of MT-1 protects against focal cerebral ischemia and reperfusion.

L51 ANSWER 2 OF 16 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD
AN 1998-261035 [23] WPIDS
AB WO 9816551 A UPAB: 19980610
New vascular endothelial growth factor (VEGF) antagonist molecule (I), comprises a variant VEGF polypeptide comprising an aa modification of at least 1 cysteine residue, where the aa modification inhibits the ability of the variant polypeptide to properly dimerise with another VEGF polypeptide monomer, and where (I) is capable of binding to VEGF receptors without significantly inducing a VEGF response, and functional derivatives

of (I). Also claimed are: (1) an isolated nucleic acid sequence encoding (I); (2) replicable expression vector capable of expressing the nucleic acid sequence in a transformant host cell, and (3) host cells, (especially
Chinese hamster ovary cells) transformed with the vector.

USE - The products can be used in the treatment of diseases or disorders characterised by undesirable excessive vascularisation, e.g. tumours, rheumatoid arthritis, psoriasis, atherosclerosis, diabetic or other retinopathies, retrolental fibroplasia, age-related macular degeneration, neovascular glycoma, haemangiomas, thyroid hyperplasias (including Grave's disease), corneal and other tissue transplantation and chronic inflammation. The products can also be used to treat diseases or disorders characterised by undesirable vascular permeability, e.g. **oedema** associated with brain tumours, ascites associated with malignancies, Meigs' syndrome, lung inflammation, nephrotic syndrome, pericardial effusion and pleural effusion.
Dwg.8/8

L51 ANSWER 3 OF 16 MEDLINE DUPLICATE 2
1998141616 Document Number: 98141616. Prevalence of varicose veins in an Italian elderly population. Canonico S; Gallo C; Paolisso G; Pacifico F; Signoriello G; Sciaudone G; **Ferrara N**; Piegari V; Varricchio M; Rengo F. (Institute of General Surgery, 2nd University of Naples, Italy.)

ANGIOLOGY, (1998 Feb) 49 (2) 129-35. Journal code: 4UA. ISSN: 0003-3197. Pub. country: United States. Language: English.

AB The prevalence of varicose veins (VV) in the elderly population of the Campania Region, in Southern Italy, was estimated. A random sample of the people aged more than 65 years was drawn by means of a stratified multistage sampling design warranting that observed percentages were direct estimates of population percentages. The investigation covered 1319
subjects, 560 (42.5%) men and 759 (57.5%) women, their ages ranging from 66 to 96 years with an average value of 74.2 years, who were interviewed and visited by trained physicians. VV were defined as any reticular or truncal visible varicosities of the lower limbs, and investigated symptoms
were heaviness, pain, nightly cramps, **edema**, eczema, hyperpigmentation, and ulceration. Some variables were studied as risk factors: age, sex, lifetime occupation, smoking, alcohol, hypertension, diabetes, and obesity; previous treatment and use of elastic stockings were also studied. Statistical associations were evaluated by Chi-square test, a two-tailed P value of 0.05 being assumed as significance level. In
total, 391 (29.6%) subjects were reported to be affected by VV, but the clinical examination was positive in only 362 (27.4%) with a good correspondence between answers and clinical findings. Prevalence was greatly affected by sex, the percentage being two times higher in women (35.2%) than in men (17%). VV developed after a pregnancy in 40.5% of women, but a high percentage of women (38.2%) also reported menopause as a
time starting point. No significant association between reported risk factors and VV was found among men, whereas obesity was strongly related to VV in women. One or more symptoms were reported in 92.1% of persons affected by VV, but no previous therapy was reported by 58.9% of subjects.
Only 16.9% of patients used elastic stockings with a significant difference between men (7.4%) and women (20.2%).

L51 ANSWER 4 OF 16 MEDLINE DUPLICATE 3
97098336 Document Number: 97098336. Intravitreous injections of vascular

endothelial growth factor produce retinal ischemia and microangiopathy in an adult primate. Tolentino M J; Miller J W; Gragoudas E S; Jakobiec F A; Flynn E; Chatzistefanou K; **Ferrara N**; Adamis A P. (Department of Ophthalmology, Massachusetts Eye and Ear Infirmary, Boston 02114, USA.) OPHTHALMOLOGY, (1996 Nov) 103 (11) 1820-8. Journal code: OI5. ISSN: 0161-6420. Pub. country: United States. Language: English.

AB PURPOSE: The purpose of the study is to determine the effect of exogenous vascular endothelial growth factor (VEGF) on the primate retina and its vasculature. METHODS: Ten eyes of five animals were studied. Physiologically relevant amounts of the 165 amino acid isoform of human recombinant VEGF were injected into the vitreous of six healthy cynomolgus monkey eyes. Inactivated human recombinant VEGF or vehicle was injected into four contralateral control subject eyes. Eyes were assessed by slit-lamp biomicroscopy, tonometry, fundus color photography, fundus fluorescein angiography, light microscopy, and immunostaining with antibodies against proliferating cell nuclear antigen and factor VIII antigen. RESULTS: All six bioactive VEGF-injected eyes developed dilated, tortuous retinal vessels that leaked fluorescein. Eyes receiving multiple injections of VEGF developed progressively dilated and tortuous vessels, venous beading, **edema**, microaneurysms, intraretinal hemorrhages and capillary closure with ischemia. The severity of the retinopathy correlated with the number of VEGF injections. None of the four control eyes exhibited any abnormal retinal vascular changes. The endothelial cells of retinal blood vessels were proliferating cell nuclear antigen positive only in the bioactive VEGF-injected eyes. CONCLUSION: Vascular endothelial growth factor is sufficient to produce many of the vascular abnormalities common to diabetic retinopathy and other ischemic retinopathies, such as hemorrhage, **edema**, venous beading, capillary occlusion with ischemia, microaneurysm formation, and intraretinal vascular proliferation.

L51 ANSWER 5 OF 16 MEDLINE DUPLICATE 4
97054414 Document Number: 97054414. Experimental cerebral venous thrombosis: evaluation using magnetic resonance imaging. Rother J; Waggie K; **van Bruggen N**; de Crespigny A J; Moseley M E. (Department of Radiology, Stanford University, California, USA.) JOURNAL OF CEREBRAL BLOOD FLOW AND METABOLISM, (1996 Nov) 16 (6) 1353-61. Journal code: HNL. ISSN: 0271-678X. Pub. country: United States. Language: English.

AB Diffusion-weighted (DWI), dynamic contrast-enhanced (perfusion imaging), and conventional spin-echo magnetic resonance imaging (MRI) were applied to characterize the pathophysiology of cerebral venous thrombosis (CVT) in the rat. We induced CVT by rostral and caudal ligation of the superior sagittal sinus (SSS) and injection of a thrombogenic cephalin suspension. The resulting pathology was monitored in an acute and long-term study group. Evans blue and hematoxylin-eosin staining was performed for comparison with MRI data. A subgroup of animals was treated with i.v. tissue plasminogen activator (t-PA). Successful thrombosis of the SSS was confirmed by macropathology or histopathology in all rats. Parenchymal lesions as shown by MRI, however, were present only in animals with additional involvement of cortical cerebral veins (11 of 18 rats). The early pathology was clearly detected with the DWI. The apparent diffusion coefficient declined to 56 +/- 7% of control value at 0.5 h and slowly increased to 84 +/- 8% by 48 h. Perfusion imaging showed parasagittal perfusion deficits. Treatment with t-PA partially resolved the hyperintensity on DWI. Evidence of blood-brain-barrier disruption was observed 2 to 3 h after induction of CVT. In conclusion, experimental CVT is characterized by early cytotoxic **edema** closely followed by

vasogenic **edema**. The t-PA treatment partially reversed the DWI signal changes consistent with regional tissue recovery, as shown by histopathology. These results encourage the use of cytoprotective drugs in addition to anticoagulant or thrombolytic therapy.

L51 ANSWER 6 OF 16 MEDLINE DUPLICATE 5
95310397 Document Number: 95310397. Identification of collaterally perfused areas following focal cerebral ischemia in the rat by comparison of gradient echo and diffusion-weighted MRI. Roussel S A; **van Bruggen N**; King M D; Gadian D G. (Royal College of Surgeons Unit of Biophysics, Institute of Child Health, London, England.) JOURNAL OF CEREBRAL BLOOD FLOW AND METABOLISM, (1995 Jul) 15 (4) 578-86. Journal code: HNL. ISSN: 0271-678X. Pub. country: United States. Language: English.

AB Diffusion-weighted (DW) and gradient echo (GE) magnetic resonance images were acquired before and after occlusion of the middle cerebral artery (MCA) in the rat. Upon occlusion, an increase in DW imaging signal intensity was observed in a core area within the MCA territory, most likely reflecting cytotoxic **edema**. The signal from GE images, which is sensitive to changes in the absolute amount of deoxyhemoglobin, decreased following ischemia within a region that extended beyond the core area observed with DW imaging. This hypointensity is attributed to increases in blood volume and/or oxygen extraction fraction, which result from a decrease in perfusion pressure in the collaterally perfused area. The evolution of the GE imaging signal intensity from different regions was studied for 3.5 h following the occlusion. In the core area, the GE imaging signal returned towards baseline values after approximately 1-2 h, while it remained stable in the surrounding area. This feature may reflect a decrease in hematocrit due to microcirculatory defect and/or a decrease in the oxygen extraction fraction due to ongoing infarction of the tissue and may indicate that tissue recovery is severely compromised. The combined use of DW and GE imaging offers great promise for the noninvasive identification of specific pathological events with high spatial resolution.

L51 ANSWER 7 OF 16 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD
AN 1994-167391 [20] WPIDS
AB WO 9410202 A UPAB: 19940705
(A) A compsn. is claimed comprising a human vascular endothelial growth factor (hVEGF) antagonist, provided however that the antagonist is not the flt or flk-1 or KOR receptor or a neutralising anti-hVEGF antibody.
Also claimed are: (B) a monoclonal antibody (MAb) amino acid sequence capable of specifically binding to a HVEGF receptor (hVEGFr) or a hVEGF-hVEGFr; (C) a polypeptide comprising an amino acid sequence comprising a bVEGFr and an immunoglobulin chain; (D) a method of treatment of a tumour in a mammal comprising administering a HVEGF antagonist to reduce the size of the tumour.
USE - The hVEGF antagonists can be used to inhibit the mitogenic, angiogenic or other biological activity of VEGF and are useful for treating disorders characterised by undesirable excessive necvascularisation such as tumours, rheumatoid arthritis, psoriasis, etc. They are also useful for the treatment of disorders characterised by undesirable excessive vascular permeability such as **oedema**

associated with brain tumours, ascites associated with malignancies, etc. The prods. are also useful in detection, diagnostic assays, in vivo imaging and screening assays for agonists or antagonists.

In an example, Balb/c mice were immunised 4 times every 2 weeks by i.p. injections with 5 mg of hVEGF conjugated to 20mg of (KLH) keyhole limpet haemocyamin and were boasted with the same dose of conjugate 4 days prior to fusion. The spleen cells were fused with P3x63 Ag 8 U.1 mycloma cells to produce a hybridoma which secreted anti-hVEGF MAb. The MAb inhibited the ability of hVEGF to support the growth or survival of bovine adrenal cortex capillary endothelial cells.

Dwg.0/10

L51 ANSWER 8 OF 16 MEDLINE DUPLICATE 6

94355164 Document Number: 94355164. The application of magnetic resonance imaging to the study of experimental cerebral ischaemia. **van Bruggen N**; Roberts T P; Cremer J E. (Royal College of Surgeons Unit of Biophysics, Institute of Child Health, London, England.) CEREBROVASCULAR AND BRAIN METABOLISM REVIEWS, (1994 Summer) 6 (2) 180-210. Ref: 151. Journal code: AVC. ISSN: 1040-8827. Pub. country: United States. Language: English.

AB Recent developments in the field of magnetic resonance imaging (MRI) have opened up new opportunities in the investigation of disease. This review seeks to illustrate how some of these advances have made MRI a powerful tool with which to study the pathology and physiology of cerebral ischaemia. Emphasis will be placed on new techniques at the disposal of the MR investigator. These include techniques to monitor alterations in cerebral blood flow and volume; diffusion-weighted imaging to investigate the acute pathology of cerebral ischaemia; and techniques sensitive to alteration in tissue blood oxygenation levels that provide a wholly noninvasive means of assessing cerebral haemodynamics, including hyperaemia and CO2 reactivity. Particular reference to the ability of such techniques to identify ischaemic tissue prior to irreversible damage will be made, and the implication for pharmaceutical research and potential therapy will be discussed. A detailed technical description of nuclear MR theory is avoided, and we have concentrated on the application of MRI to interrogate the pathophysiology of cerebral ischaemia.

L51 ANSWER 9 OF 16 MEDLINE DUPLICATE 7

93139219 Document Number: 93139219. Expression of vascular endothelial growth factor does not promote transformation but confers a growth advantage in vivo to Chinese hamster ovary cells. **Ferrara N**; Winer J; Burton T; Rowland A; Siegel M; Phillips H S; Terrell T; Keller G A; Levinson A D. (Genentech, Inc., South San Francisco, California 94080.) JOURNAL OF CLINICAL INVESTIGATION, (1993 Jan) 91 (1) 160-70. Journal code: HS7. ISSN: 0021-9738. Pub. country: United States. Language: English.

AB Vascular endothelial growth factor (VEGF) is a mitogen with a specificity for endothelial cells in vitro and an angiogenic inducer in vivo. We tested the hypothesis that VEGF may confer on expressing cells a growth advantage in vivo. Dihydrofolatereductase--Chinese hamster ovary cells were transfected with expression vectors which direct the constitutive synthesis of VEGF. Neither the expression nor the exogenous administration of VEGF stimulated anchorage-dependent or anchorage-independent growth of Chinese hamster ovary cells in vitro. However, VEGF-expressing clones, unlike control cells, demonstrated an ability to proliferate in nude mice.

Histologic examination revealed that the proliferative lesions were compact, well vascularized, and **nonedematous**. Ultrastructural analysis revealed that capillaries within the lesions were of the continuous type. These findings indicate that the expression of VEGF may confer on cells the ability to grow in vivo in the absence of transformation by purely paracrine mechanisms. Since VEGF is a widely distributed protein, this property may have relevance for a variety of physiological and pathological proliferative processes.

L51 ANSWER 10 OF 16 MEDLINE

94069627 Document Number: 94069627. Applications of NMR spectroscopy to the study of experimental stroke in vivo. Gadian D G; Allen K; **van Bruggen N**; Busza A L; King M D; Williams S R. (Royal College of Surgeons, Institute of Child Health, London, UK.) STROKE, (1993 Dec) 24 (12 Suppl) I57-9; discussion I66-8. Journal code: V2J. ISSN: 0039-2499. Pub. country: United States. Language: English.

AB BACKGROUND AND PURPOSE: Magnetic resonance spectroscopy and imaging enable us to investigate biochemical and pathophysiological changes associated with cerebral ischemia. The specific aims of these studies were to establish the relationships between energy metabolites and regional cerebral blood flow and to determine whether diffusion-weighted imaging is sensitive to the known thresholds for cerebral tissue energy failure and disturbance of transmembrane ionic gradients in gerbils. METHODS: Magnetic resonance spectroscopy measurements of energy metabolites in the gerbil brain were obtained as a function of cerebral blood flow (measured with the hydrogen clearance technique) before, during, and after unilateral or bilateral occlusion of the common carotid arteries. Diffusion-weighted and T2-weighted images were obtained in a separate series of experiments. RESULTS: Major changes in brain energy metabolites were observed at flow values of 20 ml.100 g-1.min-1 and below. The cerebral blood flow threshold for maintenance of energy status was lowered in hypothermia, consistent with a protective effect. Diffusion-weighted imaging intensity increased at cerebral blood flow values of 15 to 20 ml.100 g-1.min-1 and below and increased gradually following the onset of severe global cerebral ischemia, but with a delay of about 2.5 minutes. CONCLUSIONS: The spectroscopic observations suggest that the flow thresholds for electrical function and **edema** are a direct consequence of energy failure. Comparison of the spectroscopy and imaging data suggests that diffusion-weighted imaging is sensitive to disruption of tissue energy metabolism or to a consequence of this disruption. The possibilities arise of visualizing energy failure with the spatial resolution characteristic of magnetic resonance imaging and detecting compromised but recoverable tissue.

L51 ANSWER 11 OF 16 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.

93350071 EMBASE Document No.: 1993350071. Applications of NMR spectroscopy to the study of experimental stroke in vivo. Gadian D.G.; Allen K.; **Van Bruggen N.**; Busza A.L.; King M.D.; Williams S.R.. Unit of Biophysics, Institute of Child Health, Royal College of Surgeons, 30 Guilford Street,London WC1N 1EH, United Kingdom. Stroke 24/12 SUPPL. (I57-I59) 1993.

ISSN: 0039-2499. CODEN: SJCCA7. Pub. Country: United States. Language: English. Summary Language: English.

AB Background and Purpose: Magnetic resonance spectroscopy and imaging enable us to investigate biochemical and pathophysiological changes associated with cerebral ischemia. The specific aims of these studies were to establish the relationships between energy metabolites and regional cerebral blood flow and to determine whether diffusion-weighted imaging is sensitive to the known thresholds for cerebral tissue energy failure and disturbance of transmembrane ionic gradients in gerbils. Methods: Magnetic resonance spectroscopy measurements of energy metabolites in the gerbil brain were obtained as a function of cerebral blood flow (measured with the hydrogen clearance technique) before, during, and after unilateral or bilateral occlusion of the common carotid arteries. Diffusion-weighted and T2-weighted images were obtained in a separate series of experiments. Results: Major changes in brain energy metabolites were observed at flow values of 20 ml .cntdot. 100 g-1 .cntdot. min-1 and below. The cerebral blood flow threshold for maintenance of energy status was lowered in hypothermia, consistent with a protective effect. Diffusion-weighted imaging intensity increased at cerebral blood flow values of 15 to 20 ml .cntdot. 100 g-1 .cntdot. min-1 and below and increased gradually following the onset of severe global cerebral ischemia, but with a delay of about 2.5 minutes. Conclusions: The spectroscopic observations suggest that the flow thresholds for electrical function and **edema** are a direct consequence of energy failure. Comparison of the spectroscopy and imaging data suggests that diffusion-weighted imaging is sensitive to disruption of tissue energy metabolism or to a consequence of this disruption. The possibilities arise of visualizing energy failure with the spatial resolution characteristic of magnetic resonance imaging and detecting compromised but recoverable tissue.

L51 ANSWER 12 OF 16 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.
92168531 EMBASE Document No.: 1992168531. T2- and diffusion-weighted magnetic resonance imaging of a focal ischemic lesion in rat brain. **Van Bruggen N.**; Cullen B.M.; King M.D.; Doran M.; Williams S.R.; Gadian D.G.; Cremer J.E.. Department of Biophysics, Hunterian Institute, Royal College of Surgeons of England, 35-43 Lincoln's Inn Fields,London WC2A 3PN, United Kingdom. Stroke 23/4 (576-582) 1992.
ISSN: 0039-2499. CODEN: SJCCA7. Pub. Country: United States. Language: English. Summary Language: English.

AB Background and Purpose: We sought to evaluate the application of T2-weighted and diffusion-weighted magnetic resonance imaging techniques in the study of a focal ischemic lesion in the rat brain. Methods: Unilateral cortical infarcts were induced using the photosensitive dye rose bengal and 560 nm light irradiation. Magnetic resonance images were recorded from a total of 11 rats at selected intervals from 1.5 hours to several days after induction of the lesion. Parallel experiments were performed in which Evans blue dye was injected into the lesioned animals either immediately after lesion induction (n=11) or 1 hour before the animals were killed (n=11). The second procedure was designed to show regions of blood-brain barrier permeability to plasma proteins at the time of sacrifice, whereas the first procedure showed the accumulation and subsequent dispersion of plasma protein following disruption of the blood-brain barrier. Results: Regions of the cortex highlighted by the T2-weighted images corresponded well to the pattern of dye staining seen from the first procedure while the diffusion-weighted images showed visual

correspondence with the staining pattern obtained using the second procedure. Conclusions: These results illustrate the complementary use of T2-weighted and diffusion-weighted magnetic resonance imaging in discerning the pathophysiology of developing lesions.

L51 ANSWER 13 OF 16 BIOSIS COPYRIGHT 2000 BIOSIS
1992:204438 Document No.: BR42:97513. THE DEVELOPMENT AND PROGRESSION OF CEREBRAL **OEDEMA** AS MONITORED BY MAGNETIC RESONANCE IMAGING MRI OF ANAESTHETIZED RATS. **VAN BRUGGEN N**; CULLEN B M; KING M D; GADIAN D G; WILLIAMS S R; CREMER J E. DEP. BIOPHYSICS, HUNTERIAN INST., ROYAL COLL. SURGEONS ENGLAND, LONDON WC2A 3PN.. MEETING OF THE PHYSIOLOGICAL SOCIETY, LONDON, ENGLAND, UK, NOVEMBER 15-16, 1991. J PHYSIOL (CAMB). (1992) 446 (0), 509P. CODEN: JPHYA7. ISSN: 0022-3751. Language: English.

L51 ANSWER 14 OF 16 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.
92101227 EMBASE Document No.: 1992101227. The development and progression of cerebral **oedema** as monitored by magnetic resonance imaging (MRI) of anaesthetized rats. **Van Bruggen N.**; Cullen B.M.; King M.D.; Gadian D.G.; Williams S.R.; Cremer J.E.. Department of Biophysics, Hunterian Institute, The Royal College of Surgeons,London WC2A 3PN, United Kingdom. Journal of Physiology 446/- (509P) 1992. ISSN: 0022-3751. CODEN: JPHYA7. Pub. Country: United Kingdom. Language: English.

L51 ANSWER 15 OF 16 MEDLINE DUPLICATE 8
92048414 Document Number: 92048414. Diffusion-weighted imaging of kainic acid lesions in the rat brain. King M D; **van Bruggen N**; Ahier R G; Cremer J E; Hajnal J V; Williams S R; Doran M. (Department of Biophysics, Hunterian Institute, Royal College of Surgeons, London.) MAGNETIC RESONANCE IN MEDICINE, (1991 Jul) 20 (1) 158-64. Journal code: MHR. ISSN: 0740-3194. Pub. country: United States. Language: English.
AB We present T2-weighted and diffusion-weighted images of kainic acid lesions in the rat brain. Our observations show improved image contrast between **edematous** lesions and unaffected tissue using diffusion-weighted imaging. Furthermore, we show that the anisotropic intensity changes associated with this sequence can be used to highlight white matter tracts and to provide information concerning their orientation in the rat brain.

L51 ANSWER 16 OF 16 MEDLINE DUPLICATE 9
91213712 Document Number: 91213712. Restoration of energy metabolism and resolution of **oedema** following profound ischaemia. Allen K L; Busza A L; Proctor E; Williams S R; **Van Bruggen N**; Gadian D G; Crockard H A. (Institute of Neurology, London, U.K.) ACTA NEUROCHIRURGICA. SUPPLEMENTUM, (1990) 51 171-3. Journal code: 19E. ISSN: 0065-1419. Pub. country: Austria. Language: English.
AB Cerebral ischaemia was produced in 2 groups of gerbils by occlusion of the common carotid arteries for 30 minutes, resulting in cerebral **oedema**. In group 1 cerebral **oedema** was measured by specific gravity microgravimetry, and in group 2 brain metabolism and blood flow were measured by 31P and 1H NMR spectroscopy and hydrogen clearance respectively. In group 1 the brain water content did not return to control levels by 180 minutes of reperfusion. Energy metabolism, determined by 31P NMR spectroscopy returned to control by 12 minutes, intracellular pH (pHi) by 20 minutes, and lactate, determined by 1H NMR spectroscopy, by 50 minutes. There was a lag of about 10 minutes before lactate began to be cleared from the brain. We suggest that while pHi is low, Na+/H+ exchange will negate the Na+ extrusion driven by the Na+/K+

ATPase. When pHi approaches normal there will be a net extrusion of Na+, taking osmotic water with it, and presumably with passive washout of lactate. This may be the cause of the initial delay in lactate clearance.

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L53 0 FILE CAPLUS
L54 0 FILE BIOSIS
L55 0 FILE EMBASE
L56 0 FILE WPIDS

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L66 0 FILE BIOSIS
L67 8 FILE EMBASE
L68 0 FILE WPIDS

TOTAL FOR ALL FILES
L69 21 "EDEMA: RH, REHABILITATION"/CT

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L69 ANSWER 1 OF 21 MEDLINE
AN 1999356686 MEDLINE
DN 99356686
TI A sling support for scrotal edema.
AU Benjamin K D
CS Portland Veterans Administration Medical Center, Oregon 97207, USA.
SO AMERICAN JOURNAL OF OCCUPATIONAL THERAPY, (1999 Jul-Aug) 53 (4) 392-3.
Journal code: 3O4. ISSN: 0272-9490.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199910
EW 19991002

=> e

E157 2724 EDEMA: SI, SIDE EFFECT/CT
E158 448 EDEMA: SU, SURGERY/CT
E159 997 EDEMA: TH, THERAPY/CT
E160 1 EDEMA: TM, TRANSMISSION/CT
E161 48 EDEMA: UR, URINE/CT

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E162          98            EDEMA: US, ULTRASONOGRAPHY/CT
E163         406            EDEMA: VE, VETERINARY/CT
E164           7            EDEMA: VI, VIROLOGY/CT
E165           0      2     EDEMAS/CT
E166           0      2     EDEMAS, ANGIONEUROTIC/CT
E167           0      2     EDEMAS, CARDIAC/CT
E168           0      2     EDEMAS, CORNEAL/CT

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L73          156 FILE EMBASE
L74            0 FILE WPIDS

TOTAL FOR ALL FILES
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E170           0      2     EDEMAS, FETAL/CT
E171           0      2     EDEMAS, LARYNGEAL/CT
E172           0      2     EDEMAS, OPTIC DISK/CT
E173           0      2     EDEMAS, OPTIC PAPILLA/CT
E174           0      2     EDEMAS, PULMONARY/CT
E175           0      2     EDEMAS, RETINAL/CT
E176           1            EDEMATIC/CT
E177           1            EDEMATIZATION/CT
E178           1            EDEMATOGENIC ACTIVITY/CT
E179           1            EDEMATOLYSIN/CT
E180           6            EDEMATOUS/CT

=> e vegf/ct

E#   FREQUENCY    AT      TERM
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E1           1            VEGETEX/CT
E2           1            VEGETOTROPIC SUBSTANCE/CT
E3         234     1 --> VEGF/CT
E4          76            VEGF (VASCULAR ENDOTHELIAL GROWTH FACTOR)/CT
E5           1            VEGF 115/CT
E6           1            VEGF 165 GENE/CT
E7           1            VEGF ANTAGONIST/CT
E8           1            VEGF ANTIBODY/CT
E9           1            VEGF ANTIBODY (VASCULAR ENDOTHELIAL GROWTH FACTOR
ANTI
                          BODY)/CT
E10          1            VEGF ANTIBODY: CT, CLINICAL TRIAL/CT
E11          1            VEGF ANTIBODY: DT, DRUG THERAPY/CT
E12          1            VEGF ANTIBODY: PD, PHARMACOLOGY/CT

=> e anti vegf/ct

E#   FREQUENCY    AT      TERM
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E1           0     2      ANTI VARICOSITY AGENT/CT
E2           1            ANTI VCAM-1 ANTIBODY/CT
E3           2       --> ANTI VEGF/CT
E4           1            ANTI VEGF: CB, DRUG COMBINATION/CT
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E5            2           ANTI VEGF: DV, DRUG DEVELOPMENT/CT
E6            2           ANTI VEGF: PD, PHARMACOLOGY/CT
E7            2           ANTI VEL/CT
E8            1           ANTI VIMENTINE ANTIBODIES/CT
E9            0     2     ANTI VIRAL/CT
E10           0     2     ANTI VIRAL AGENT/CT
E11           1           ANTI VIRAL PROTEIN KINASE/CT
E12           0     2     ANTI VIRUS VACCINE/CT

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L77           0 FILE CAPLUS
L78           0 FILE BIOSIS
L79           2 FILE EMBASE
L80           0 FILE WPIDS

TOTAL FOR ALL FILES
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"ANTI
                VEGF: DV, DRUG DEVELOPMENT"/CT OR "ANTI VEGF: PD,
PHARMACOLOGY"
               /CT)

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L84           0 FILE BIOSIS
L85           0 FILE EMBASE
L86           0 FILE WPIDS

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L87           0 L81 AND (L75 OR L69 OR L63)

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COST IN U.S. DOLLARS                          SINCE FILE      TOTAL
                                                 ENTRY     SESSION
FULL ESTIMATED COST                              71.26       71.71

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CANCERLIT, CAPLUS, CEABA, CEN, CIN, CONFSCI, CROPB, CROPU, DDFB, DDFU, DGENE, DRUGB, DRUGLAUNCH, DRUGMONOG2, ...' ENTERED AT 16:54:06 ON 24 MAY 2000

SEA GLIOBLASTOMA(10W)EDEMA

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1 FILE DDFU
2 FILE DRUGU
6 FILE EMBASE
1 FILE ESBIOBASE
3 FILE JICST-EPLUS
7 FILE MEDLINE
4 FILE SCISEARCH
2 FILE USPATFULL

L1 QUE GLIOBLASTOMA(10W) EDEMA

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(FILE 'HOME' ENTERED AT 16:53:19 ON 24 MAY 2000)

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CANCERLIT, CAPLUS, CEABA, CEN, CIN, CONFSCI, CROPB, CROPU, DDFB, DDFU, DGENE, DRUGB, DRUGLAUNCH, DRUGMONOG2, ...' ENTERED AT 16:54:06 ON 24 MAY 2000

SEA GLIOBLASTOMA(10W)EDEMA

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2 FILE DRUGU
6 FILE EMBASE
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3 FILE JICST-EPLUS
7 FILE MEDLINE
4 FILE SCISEARCH
2 FILE USPATFULL

L1 QUE GLIOBLASTOMA(10W) EDEMA

FILE 'BIOSIS, CANCERLIT, MEDLINE, EMBASE, SCISEARCH, JICST-EPLUS, DRUGU, USPATFULL, CAPLUS, ESBIOBASE' ENTERED AT 16:59:16 ON 24 MAY 2000

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L3 20 DUP REM L2 (21 DUPLICATES REMOVED)